Li, B.
10/028172

(FILE 'REGISTRY' ENTERED AT 15:45:49 ON 15 MAY 2002)
E BOVINE SERUM ALBUMIN/CN 5
L3 3 S BOVINE SERUM ALBUMIN ?/CN
E OVALBUMIN/CN 5
L4 8 S OVALBUMIN ?/CN
E HEMOCYANIN/CN 5
L5 71 S HEMOCYANIN ?/CN
L6 82 S L3 OR L4 OR L5

E POLYSTYRENE LATEX/CN 5
L10 1 S E3

FILE 'CAPLUS' ENTERED AT 15:51:33 ON 15 MAY 2002
L1 8932 SEA FILE=CAPLUS ABB=ON PLU=ON HCV OR HEPATIT?(3A)C
L2 2153 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND ANTIGEN
L3 3 SEA FILE=REGISTRY ABB=ON PLU=ON BOVINE SERUM ALBUMIN ?/CN
L4 8 SEA FILE=REGISTRY ABB=ON PLU=ON OVALBUMIN ?/CN
L5 71 SEA FILE=REGISTRY ABB=ON PLU=ON HEMOCYANIN ?/CN
L6 82 SEA FILE=REGISTRY ABB=ON PLU=ON L3 OR L4 OR L5
L7 211 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (L6 OR CARRIER OR BSA OR BOVINE(1W)ALBUMIN OR OVALBUMIN OR HEMOCYANIN OR HAEMOCYANIN OR (HEMO OR HAEMO)(W)CYANIN)
L8 115 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN?)
L9 15 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND CONJUGAT?

L1 8932 SEA FILE=CAPLUS ABB=ON PLU=ON HCV OR HEPATIT?(3A)C
L2 2153 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND ANTIGEN
L3 3 SEA FILE=REGISTRY ABB=ON PLU=ON BOVINE SERUM ALBUMIN ?/CN
L4 8 SEA FILE=REGISTRY ABB=ON PLU=ON OVALBUMIN ?/CN
L5 71 SEA FILE=REGISTRY ABB=ON PLU=ON HEMOCYANIN ?/CN
L6 82 SEA FILE=REGISTRY ABB=ON PLU=ON L3 OR L4 OR L5
L7 211 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND (L6 OR CARRIER OR BSA OR BOVINE(1W)ALBUMIN OR OVALBUMIN OR HEMOCYANIN OR HAEMOCYANIN OR (HEMO OR HAEMO)(W)CYANIN)
L8 115 SEA FILE=CAPLUS ABB=ON PLU=ON L7 AND (DIAGNOS? OR DETERM? OR DETECT? OR DET## OR SCREEN?)
L10 1 SEA FILE=REGISTRY ABB=ON PLU=ON "POLYSTYRENE LATEX"/CN
L11 9 SEA FILE=CAPLUS ABB=ON PLU=ON L8 AND (L10 OR POLYSTYRENE OR LATEX OR POLY STYRENE OR (HYDROPHOB? OR HYDROPHOB?)(5A)(SUBSTANC? OR MATERIAL OR PARTICLE))

L12 21 L9 OR L11

L12 ANSWER 1 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:915415 CAPLUS
DOCUMENT NUMBER: 136:4697
TITLE: Rapid joint assay method for viral antibodies of AIDS and **hepatitis C**
INVENTOR(S): Zhou, Siliang
PATENT ASSIGNEE(S): Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 22 pp.

CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1305109	A	20010725	CN 2001-107196	20010227

AB The rapid immunoassay for simultaneous **detection** of viral antibodies of AIDS and **hepatitis C** is presented. The test strip of nitrocellulose membrane consists of AIDS viral **antigen, HCV antigen,** and low- and high-concn. dinitrophenol as contrast. The marker is the color matter such as colloidal Au-labeled **conjugate** of anti-dinitrophenol antibody and rabbit-anti-human gamma-globulin antibody in buffer I. The coating buffer is composed of KCl, NaCl, K2HPO4, and Na2HPO4. The buffer I is composed of KCl, NaCl, K2HPO4, NaH2PO4, casein, **bovine** serum **albumin,** NaN3 , Tween-20, and EDTA. The sealing buffer is composed of KCl, NaCl, K2HPO4, Na2HPO4, **bovine** serum **albumin,** Triton X-100, polyvinyl pyrrolidone, sucrose and gamma-globulin.

L12 ANSWER 2 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:343429 CAPLUS
DOCUMENT NUMBER: 135:119408
TITLE: Evidence for a new **Hepatitis C** virus **antigen** encoded in an overlapping reading frame
AUTHOR(S): Walewski, Jose L.; Keller, Toby R.; Stump, Decherd D.; Branch, Andrea D.
CORPORATE SOURCE: Division of Liver Diseases, Department of Medicine, Mount Sinai School of Medicine, New York, NY, 10029, USA
SOURCE: RNA (2001), 7(5), 710-721
CODEN: RNARFU; ISSN: 1355-8382
PUBLISHER: Cambridge University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Many viruses have overlapping genes and/or regions in which a nucleic acid signal is embedded in a coding sequence. To search for dual-use regions in the **hepatitis C** virus (**HCV**), we developed a facile computer-based sequence anal. method to map dual-use regions in coding sequences. Eight diverse full-length **HCV** RNA and polyprotein sequences were aligned and analyzed. A cluster of unusually conserved synonymous codons was found in the core-encoding region, indicating a potential overlapping open reading frame (ORF). Four peptides (A1, A2, A3, and A4) representing this alternate reading frame protein (ARFP), two others from the **HCV** core protein, and one from **bovine** serum **albumin** (**BSA**) were **conjugated** to **BSA** and used in western blots to test sera for specific antibodies from 100 chronic **HCV** patients, 44 healthy controls, and 60 patients with non-**HCV** liver disease. At a 1:20,000 diln., specific IgGs to three of the four ARFP peptides were **detected** in chronic **HCV** sera. Reactivity to either the A1 or A3 peptides (both ARFP derived) was significantly assocd. with chronic **HCV**

infection, when compared to non-**HCV** liver disease serum samples (10/100 vs. 1/60; $p < 0.025$). Antibodies to A4 were not **detected** in any serum sample. Our western blot assays confirmed the presence of specific antibodies to a new **HCV antigen** encoded, at least in part, in an alternate reading frame (ARF) overlapping the core-encoding region. Because this novel **HCV** protein stimulates specific immune responses, it has potential value in **diagnostic** tests and as a component of vaccines. This protein is predicted to be highly basic and may play a role in **HCV** replication, pathogenesis, and carcinogenesis.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:50845 CAPLUS
DOCUMENT NUMBER: 134:130253
TITLE: Induction of a Th1-like response in vitro
INVENTOR(S): Siegel, Marvin; Chu, N. Randall; Mizzen, Lee A.
PATENT ASSIGNEE(S): Stressgen Biotechnologies Corporation, Can.
SOURCE: PCT Int. Appl., 88 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001004344	A2	20010118	WO 2000-US18828	20000710
WO 2001004344	A3	20011115		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1196772	A2	20020417	EP 2000-945300	20000710
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-143757P P 19990708
WO 2000-US18828 W 20000710

AB The invention provides compns. and methods for stimulating a Th1-like response in vitro. Compns. include fusion proteins and **conjugates** that contain at least a portion of a heat shock protein. A Th1-like response can be elicited by contacting in vitro a cell sample contg. naive lymphocytes with a fusion protein or **conjugate** of the invention. The Th1-like response can be **detected** by measuring IFN-gamma produced by the cell sample.

L12 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:835203 CAPLUS
DOCUMENT NUMBER: 134:16522

TITLE: Peptides for **detecting** anti-**hepatitis C** virus antibody
INVENTOR(S): Yokoi, Masayuki; Akamine, Takayuki
PATENT ASSIGNEE(S): Sekisui Chemical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000327698	A2	20001128	JP 1999-141760	19990521

AB Disclosed is a method and reagent for **detection** of anti-**HCV** antibody. The reagent comprises insol. **carrier**-immobilized **antigen** epitope peptide for **detecting** **HCV** antibody.

L12 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:739579 CAPLUS
DOCUMENT NUMBER: 133:308990
TITLE: Particle-immobilized antibody or **antigen** for immuno-**detection** of **antigen** or antibody
INVENTOR(S): Munebayashi, Takaaki; Ifuku, Yasuo; Nagaike, Kazuhiro
PATENT ASSIGNEE(S): Mitsubishi Chemical Corp., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 12 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000292424	A2	20001020	JP 1999-102323	19990409

AB Insol. magnetic particles contg. analyte-specific antibody and nonspecific binding biosubstances are prepd. for immunoassay of **antigen** analyte in biol. samples. The nonspecific binding biosubstances include animal proteins, amino acids, high mol. wt org. substances, and/or carbohydrates, e.g. **bovine** serum **albumin**, rabbit IgG, glycine, and dextran. The **antigen** analyte is selected from .alpha.-fetoprotein, carcinoembryonic **antigen**, hepatitis B surface **antigen**, **hepatitis C** virus **antigen**, and CA19-9 **antigen**.
IT **9003-53-6**, **Polystyrene**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(magnetic particle-immobilized antibody for **antigen** immunoassay)

L12 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:275313 CAPLUS
DOCUMENT NUMBER: 132:313670
TITLE: Coated substrates for blood, plasma, or tissue

washing and columns equipped with these substrates
INVENTOR(S): Dunzendorfer, Udo; Will, Gottfried
PATENT ASSIGNEE(S): Germany
SOURCE: Ger. Offen., 30 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19845286	A1	20000427	DE 1998-19845286	19981001
EP 1004598	A2	20000531	EP 1999-118541	19990918
EP 1004598	A3	20000607		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.: DE 1998-19845286 19981001

AB Columns, filters, cannulas, etc. contg. substrates coated with specific antibodies can be used during plasmapheresis to remove pathogenic cytokines such as tumor necrosis factor (TNF), anti-TNF, fragments of TNF or anti-TNF, or TNF transport proteins from blood, plasma, or tissues. The substrates may addnl. be coated with antibodies to microbial or viral pathogens or mixts. of pathogens as well as to polysaccharide **antigens**, viral capsids, microbial **antigens**, reverse transcriptase, endothelin, protein A, etc. Selective removal of these pathogens, **antigens**, proteins, etc. leaves all normal plasma components unchanged and obviates the need for supplementation of the plasma with these components. Suitable substrates include polymers, polymer-coated metals, cellulose derivs., starch, and Sepharose; these may be derivatized for covalent binding of the pathogens or pathogenic mols. Thus, Escherichia coli pyelonephritis was successfully treated by plasmapheresis coupled with columns loaded with anti-TNF-.alpha. for 14 days, 4 h/day, as **detd**. by decreases in plasma TNF-.alpha. levels and colony counts in urine cultures.

IT **9003-53-6, Polystyrene**
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**carrier**; coated substrates for blood, plasma, or tissue washing and columns equipped with these substrates)

L12 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:811571 CAPLUS
DOCUMENT NUMBER: 132:22168
TITLE: Improvement of binding assays by multi-epitope analysis and combination of **antigen** and antibody **determination**
INVENTOR(S): Karl, Johann; Hornauer, Hans
PATENT ASSIGNEE(S): Roche Diagnostics G.m.b.H., Germany
SOURCE: Ger. Offen., 14 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19838802	A1	19991223	DE 1998-19838802	19980826
WO 9967643	A1	19991229	WO 1999-EP4310	19990622
W: JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1090298	A1	20010411	EP 1999-931132	19990622
R: AT, CH, DE, ES, FR, GB, IT, LI, NL				

PRIORITY APPLN. INFO.: DE 1998-19827714 A1 19980622
DE 1998-19838802 A 19980826
WO 1999-EP4310 W 19990622

AB The invention discusses a method for **detection** of analytes in a described probe comprising the following steps: (a) prep. an immobile phase which comprises a nonporous **carrier** and at least two spatially sepd. test surfaces, whereby the test surfaces contain at times different, immobilized, anal. specific receptors, (b) bring the probe into contact with the immobile phase and a second analyte-specific receptor, which bears a signal transmitting group or is capable of binding with a signal transmitting group and (c) **detection** of the presence and/or the quantity of the analyte by **detn.** of the signal transmitting group on the immobile phase. The examples discuss the test for anti-HIV antibodies with several **antigen**-specific test surfaces using microspot technol., comparison of anti-HIV antibody tests in microspot format to conventional methods, comparison of combined **detn.** of HIV p24 **antigen** as well as anti-gp41 and anti-RT antibodies in microspot format to conventional methods, combined **detn.** of p24 **antigen** and anti-p24 antibody using the reverse titrn. principle, and improvement of test specificity through test surface-specific cut-off calcn.

IT **9003-53-6**, Polystyrol
RL: AMX (Analytical matrix); ANST (Analytical study)
(improvement of binding assays by multi-epitope anal. and combination of viral **antigen** and antibody **detn**
.)

L12 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:449180 CAPLUS
DOCUMENT NUMBER: 131:129038
TITLE: Immobilization of **antigen** or antibody on **carrier** or solid support for immunoassay
INVENTOR(S): Kumasawa, Toshiaki; Tagami, Hiroaki; Kitani, Yoshiyasu
PATENT ASSIGNEE(S): SRL K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11194128	A2	19990721	JP 1997-368018	19971227

AB Solid support or **carrier** is treated with water-sol. org.

solvent for immobilization of **antigen** or antibody. The water-sol. org. solvent is propanol, and the solid support is multi-well microplate of **polystyrene**. Thus, **polystyrene** microplate was treated with 2-propanol for immobilization of **hepatitis C** virus core **antigen** for **detecting** serum antibody specific for **HCV** core **antigen**.

IT **9003-53-6, Polystyrene**
RL: ARU (Analytical role, unclassified); DEV (Device component use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(immobilization of **antigen** or antibody on **carrier** or solid support for immunoassay)

L12 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:113881 CAPLUS
DOCUMENT NUMBER: 130:181472
TITLE: Method for **detecting** HBcAg from hepatitis B virus
INVENTOR(S): Liao, Jaw-Ching; Wang, Cheng-Nan
PATENT ASSIGNEE(S): Bionova Corporation, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906837	A1	19990211	WO 1998-US15849	19980728
W: DE, GB				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6153392	A	20001128	US 1998-115350	19980714
PRIORITY APPLN. INFO.:			US 1997-54194P P	19970730
			US 1998-115350 A	19980714

AB A complex comprised of the HBcAg and an albumin or an unprocessed structural protein from a pos. stranded RNA virus. The pos. stranded RNA virus is selected from Togaviridae, Coronaviridae, Retroviridae, Picornaviridae, Caliciviridae and flaviviridae, **hepatitis C** virus, HIV, and HTLV. The albumin is selected from human serum albumin, .alpha.-fetoprotein, **bovine** serum **albumin**, fetal calf serum albumin, newborn **bovine** serum **albumin** and mouse serum albumin. Pursuant to such complexing, the antigenicity of the HBcAg is enhanced when compared to HBcAg alone, in terms of both or either affinity or specificity. This complexed HBcAg can be recognized by the immune system, which produces antibodies that have a high specificity and affinity for the complexed HBcAg, although such antibodies typically do also bind the uncomplexed **antigen** to a lower specificity and affinity. Also, methods and devices using the same.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:42620 CAPLUS
DOCUMENT NUMBER: 130:92468
TITLE: Methods for covalent immobilization of biomolecules to a **carrier** by means of a His-tag
INVENTOR(S): Bosman, Alfons; Van Wijnendaele, Frans; Van Den Broeck, Dirk; Van De Voorde, Andre
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: PCT Int. Appl., 34 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9900670	A1	19990107	WO 1998-EP3883	19980625
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9887290	A1	19990119	AU 1998-87290	19980625
EP 991944	A1	20000412	EP 1998-938647	19980625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: EP 1997-870095 19970625
WO 1998-EP3883 19980625

AB The present invention relates to methods for covalent immobilization of biomols. to **carriers** and membranes, wherein the presence of a His-tag is exploited, and wherein the amino acid residues that comprise said His-tag are directly involved in the covalent bond. The present invention also provides several strategies that further augment the probability of covalent immobilization through said His-tags, such as improving the presentation of said His-tag, choosing the appropriate reaction conditions such as pH, temp., concn. of reagent and kinetics, increasing contact between His-tag and reactive groups of said **carrier** or membrane, by for instance the use of IDA or anti-His antibodies or increasing the hydrophobicity of the membrane, or shielding the rest of the biomol. from reaction by for instance increasing the hydrophobicity of said **carrier** or membrane or addn. of substrate or competitors or blocking otherwise reactive groups, or by choosing chem. reactions that have a high selectivity for histidine residues. A **carrier** can also be another biomol. The present invention thus also relates to a method that allows covalent crosslinking between identical or different biomols. When such biomols. have a natural tendency to interact with each other to form homo- or heterodimers, a strategy of increasing contact between the reactive groups (two His-tags or one His-tag and another reactive group) can be exploited. The present invention also relates to a method of providing a simultaneous and universal system for **detection** of biomols. through said

His-tag.
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECCRD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L12 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:321594 CAPLUS
DOCUMENT NUMBER: 128:293957
TITLE: Preparation of HIV **antigen** and **hepatitis C** virus **antigen** for simultaneous **determination** of anti-HIV and anti-**HCV** antibodies
INVENTOR(S): Zhu, Youming; Wang, Meiling; Han, Jinxiang
PATENT ASSIGNEE(S): Zhu, Youming, Peop. Rep. China
SOURCE: Faming Zhuanli Shenqing Gongkai Shuomingshu, 6 pp.
CODEN: CNXXEV
DOCUMENT TYPE: Patent
LANGUAGE: Chinese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1140090	A	19970115	CN 1995-110529	19950707
CN 1062662	B	20010228		

AB HIV-1 and HIV-2 **antigens** and **HCV** **antigens** are coated on **carrier** of **polystyrene**, polyethylene, cellulose, nitrocellulose, cellulose acetate, glass material or cell. The **carrier** -immobilized **antigens** are used for simultaneous **detn.** of antibodies to HIV-1/2 and **HCV** and for simultaneous **diagnosis** of HIV and **HCV** infections.

IT **9003-53-6, Polystyrene**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(prepn. of **carrier**-immobilized HIV **antigen** and **hepatitis C** virus **antigen** for simultaneous **detection** of anti-HIV and anti-**HCV** antibodies)

L12 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:743751 CAPLUS
DOCUMENT NUMBER: 128:47287
TITLE: **C** type **hepatitis** virus disease **diagnostic** agent
INVENTOR(S): Takahama, Yoichi; Shiraishi, Junichi
PATENT ASSIGNEE(S): Toa Medical Electronics Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

JP 09297141	A2	19971118	JP 1996-112442	19960507
US 6379886	B1	20020430	US 1997-850328	19970502
EP 806669	A2	19971112	EP 1997-107368	19970505
EP 806669	A3	19971126		
EP 806669	B1	20020410		
R: BE, DE, FR, GB, IT				
CN 1170875	A	19980121	CN 1997-109798	19970506

PRIORITY APPLN. INFO.: JP 1996-112442 A 19960507

AB **Hepatitis C** virus **antigen** or **carrier** protein **conjugate** is coated on a solid support and used for **detecting** anti-**hepatitis C** virus antibody and for **diagnosing HCV** infection. The **HCV antigen** is core **antigen**, NS3 **antigen**, NS4 **antigen**, or NS5 **antigen**, and the **carrier** protein is **bovine** serum **albumin**, egg white albumin or **hemocyanin**.

IT **9003-53-6, Polystyrene**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(**latex**; **C** type **hepatitis** virus disease **diagnostic** agent)

L12 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:402060 CAPLUS
DOCUMENT NUMBER: 125:112752
TITLE: Preparation of chicken egg yolk-derived antibody against **hepatitis C** virus **antigen** for **diagnosis** and therapy
INVENTOR(S): Hachiman, Takeshi; Myoshi, Hiroshi; Chiba, Tooru; Pponda, Yoshikazu; Seki, Makoto; Yamada, Suguru
PATENT ASSIGNEE(S): Shinetsu Chem Ind Co, Japan; Mitsubishi Chem Corp
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08127596	A2	19960521	JP 1994-264807	19941028

AB Antibody against **hepatitis C** virus (**HCV**) **antigen** is prepd. by immunizing chicken with recombinant **HCV antigen** peptide **conjugated** to a protein **carrier** and harvesting antibody from yolk of egg laid by the immunized chicken. The antibody is useful for **diagnosis**, prevention and treatment of **hepatitis C** virus infection.

L12 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:828611 CAPLUS
DOCUMENT NUMBER: 123:222328
TITLE: Interference-reducing agents for use in immunoassays

INVENTOR(S): Kientsch-Engel, Rosemarie; Donie, Frederic; Wiedmann, Michael
PATENT ASSIGNEE(S): Boehringer Mannheim G.m.b.H., Germany
SOURCE: Ger. Offen., 12 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 4407423	A1	19950907	DE 1994-4407423	19940305
WO 9523800	A1	19950908	WO 1995-EP690	19950225
W: CA, CN, FI, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 697021	A1	19960221	EP 1995-909783	19950225
EP 697021	B1	20000705		
R: AT, BE, DE, DK, ES, FR, GB, GR, IE, IT, NL, PT				
JP 08508301	T2	19960903	JP 1995-522680	19950225
JP 2750003	B2	19980513		
AT 194349	E	20000715	AT 1995-909783	19950225
CA 2184386	AA	19950908	CA 1995-2184386	19950303
WO 9523801	A1	19950908	WO 1995-EP776	19950303
W: CA, CN, FI, JP, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 749435	A1	19961227	EP 1995-912194	19950303
EP 749435	B1	20001011		
R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, PT, SE				
CN 1143368	A	19970219	CN 1995-191975	19950303
JP 09510289	T2	19971014	JP 1995-522705	19950303
JP 3027770	B2	20000404		
AT 196906	E	20001015	AT 1995-912194	19950303
ES 2152392	T3	20010201	ES 1995-912194	19950303
FI 9603461	A	19960904	FI 1996-3461	19960904
US 5863740	A	19990126	US 1996-700435	19960905
US 5952185	A	19990914	US 1997-958870	19971027

PRIORITY APPLN. INFO.:
DE 1994-4407423 A 19940305
WO 1995-EP690 W 19950225
WO 1995-EP776 W 19950303
US 1995-535072 B1 19951103

AB The finding concerns interference-reducing agents for avoiding nonspecific reactions in immunoassays wherein the agents used are avidin or streptavidin or their derivs. Interferences in heterogeneous immunoassays can decrease sensitivity and specificity and even cause false-pos. anal. results esp. in the **detn.** of antibodies. The agents can be used for improving immunoassays of, e.g., haptens, **antigens**, or antibodies in, e.g., body fluids. Examples are given of the prepn. of, e.g., crosslinked streptavidin after activation by various crosslinking agents, of **bovine** serum **albumin**-streptavidin **conjugates**, etc.

L12 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:810853 CAPLUS
DOCUMENT NUMBER: 123:222327

TITLE: Procedure for synthesis of antigenic peptides able to **detect** antibodies to **hepatitis C** virus in blood serum of infected persons
INVENTOR(S): Berasain Lasarte, Carmen; Riezu-Boj, Jose Ignacio; Prieto Valtuna, Jesus; Borras Cuesta, Francisco
PATENT ASSIGNEE(S): Instituto Cientifico y Tecnologico de Navarra, S.A., Spain
SOURCE: Span., 15 pp
CODEN: SPXXAD
DOCUMENT TYPE: Patent
LANGUAGE: Spanish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ES 2069476	A1	19950501	ES 1993-1361	19930618
ES 2069476	B1	19960101		

PRIORITY APPLN. INFO.: ES 1991-1525 19910628

AB Synthetic peptides suitable for use in **detection** of anti-**hepatitis C** virus antibodies in human blood serum can be prepd. which are built up with one or more of the following sequences: (A) AlaPheAlaSerArgGlyAsnHisValSerProThrHisTyrVal, (B) ThrAsnArgArgProGlnAspValLysPheProGlyGlyGlyVal, (C) LysProGlnArgLysThrLysArgAsnThrASnArgArgProVal. These sequences may be joined (1) to a lysine backbone in which the .alpha.- and .epsilon.-amino groups are substituted with other lysines, and in which the connection between peptides A, B, and C and the lysine backbone involves the free amino groups of the lysine backbone and the terminal carboxyl groups of the peptides; (2) to **bovine** serum **albumin** or other protein of high mol. wt. in which the connection between the protein and peptides A, B, or C involves the carboxyl termini of the peptides with .epsilon.-amino groups of the protein, or between any reactive free groups present in any of the peptides; or (3) joined to themselves as homo- or heteropolymers. An assay kit is described for an ELISA-type **detection** of antibodies to **hepatitis C** virus.

L12 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:785008 CAPLUS
DOCUMENT NUMBER: 123:164653
TITLE: Nucleotide-directed assembly of bimolecular and multimolecular drugs and devices
INVENTOR(S): Cubicciotti, Roger S.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9516788	A1	19950622	WO 1994-US14575	19941215

W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN
RW: KE, MW, SD, SZ, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9513736	A1	19950703	AU 1995-13736	19941215
AU 692212	B2	19980604		
EP 736103	A1	19961009	EP 1995-904932	19941215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09506629	T2	19970630	JP 1994-516992	19941215
US 5656739	A	19970812	US 1995-487959	19950607
US 5739305	A	19980414	US 1995-487968	19950607
US 5756296	A	19980526	US 1995-575781	19951222
PRIORITY APPLN. INFO.:			US 1993-169517	19931217
			WO 1994-US14575	19941215

AB This invention relates to methods and structures for coupling the activities of .gtoreq.2 mols. or groups of mols., preferably mols. with defined activities, to perform functions dependent on the spatial proximity of the constituent mols. The invention provides a method for assembling selected mols. in a single structure by use of synthetic heteropolymers or multivalent heteropolymeric hybrid structures comprised of hybridizably linked synthetic heteropolymers. Each synthetic heteropolymer comprises nucleotides having at least a 1st and a 2nd defined sequence segment. One defined sequence segment of a synthetic heteropolymer or multivalent heteropolymeric hybrid structure can specifically bind to a selected nonoligonucleotide mol. or group of mols., preferably a receptor, ligand, or effector mol. The other defined sequence segments are capable of either specifically binding to a different nonoligonucleotide mol. or group of mols. or of hybridization.

L12 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:558219 CAPLUS
DOCUMENT NUMBER: 119:158219
TITLE: Reagent and method for **detecting** **hepatitis C** virus antibody
INVENTOR(S): Ishibashi, Kaichiro; Ito, Masao; Yoshida, Iwao; Takamizawa, Akihisa; Shibatani, Takeji
PATENT ASSIGNEE(S): Eiken Kagaku K. K., Japan; Research Foundation for Microbial Diseases, Osaka University; Tanabe Seiyaku Co., Ltd.
SOURCE: PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9307488	A1	19930415	WO 1992-JP1276	19921002
W: CA, KR, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
JP 05307040	A2	19931119	JP 1992-68695	19920326
EP 642023	A1	19950308	EP 1992-920915	19921002
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL				

CN 1078805 A 19931124 CN 1993-103606 19930325
PRIORITY APPLN. INFO.: JP 1991-255524 19911002
JP 1992-68695 19920326
WO 1992-JP1276 19921002
OTHER SOURCE(S): MARPAT 119:158219
AB A reagent for **detecting** antibody to **hepatitis C** virus (**HCV**) uses as an **antigen** a peptide contg. the sequence Arg-Xaa-Gly-Pro-Arg-Leu-Gly-Arg-Arg-Pro (Xaa = amino acid, esp. Leu, Lys, Arg) from an epitope of **HCV** structural region (core **antigen**). The reagent allows specific **detection** of antibodies against the **HCV** structural region at a high **detection** rate, whereby **HCV** infection can be tested accurately at an early stage. The peptide can readily be chem. synthesized. Thus, **HCV** antibody in serum was **detd.** by ELISA using a peptide-sensitized plate and peroxidase-labeled anti-human IgG monoclonal antibody.

L12 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:515326 CAPLUS
DOCUMENT NUMBER: 119:115326
TITLE: Immunoreactive **hepatitis C** virus polypeptide compositions
INVENTOR(S): Weiner, Amy J.; Houghton, Michael
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9306126	A1	19930401	WO 1992-US7683	19920911
W: AU, BG, CA, CS, FI, HU, JP, PL, RO, RU				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9226436	A1	19930427	AU 1992-26436	19920911
AU 679429	B2	19970703		
EP 608261	A1	19940803	EP 1992-919917	19920911
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, SE				
JP 06511149	T2	19941215	JP 1992-506119	19920911
HU 67342	A2	19950328	HU 1994-741	19920911
PL 171489	B1	19970530	PL 1992-302729	19920911
PL 171972	B1	19970731	PL 1992-313797	19920911
RU 2136311	C1	19990910	RU 1994-24561	19920911
RO 116199	B1	20001130	RO 1994-391	19920911
FI 9401199	A	19940427	FI 1994-1199	19940314
US 5756312	A	19980526	US 1994-231368	19940419
US 5670152	A	19970923	US 1995-440103	19950512
US 5670153	A	19970923	US 1995-440542	19950512
US 5766845	A	19980616	US 1995-440210	19950512
US 5728520	A	19980317	US 1995-471498	19950606
US 6303292	B1	20011016	US 1998-46604	19980324

PRIORITY APPLN. INFO.: US 1991-759575 A 19910913
WO 1992-US7683 A 19920911
US 1994-231368 A3 19940419

AB Immunoreactive polypeptides comprising **hepatitis C** virus (**HCV**) epitopes, their use in vaccines and in assays and kits to **detect** antibodies to **HCV**, and methods of making them are disclosed. The E2/NS1 gene from a patient with chronic hepatitis was partially sequenced during 2 distinct episodes of hepatitis .apprx.2yr apart. The deduced amino acid sequences of the hypervariable (HV) region were strikingly different only between amino acids 391-408, with 7/8 changes occurring between amino acids 398-407. Specific 12-mer peptides were synthesized and reacted with blood plasma samples from the 2 time periods. The data indicate that while the patient developed antibodies to the HV region of the 1st variant, which were still **detectable** 2 yr later, no **detectable** humoral response had developed to the later variant which was predominant during the 2nd episode of hepatitis. Diphtheria toxoid **carrier** was activated with 6-maleimido-caproic acid N-hydroxysuccinimide ester and coupled to **HCV** peptides (384-411 and 225-260). The **conjugates** were formulated in vaccines.

L12 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1993:37469 CAPLUS
DOCUMENT NUMBER: 118:37469
TITLE: Basic structural immunogenic polypeptides having epitopes for **hepatitis C** virus, antibodies, polynucleotide sequence, vaccines, and methods
INVENTOR(S): Kotwal, Girish J.; Baroudy, Bahige M.
PATENT ASSIGNEE(S): Gamble, James N., Institute of Medical Research, USA
SOURCE: PCT Int. Appl., 244 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9212992	A2	19920806	WO 1992-US356	19920114
WO 9212992	A3	19930318		
W: AT, AU, BG, BR, CA, CH, CS, DE, ES, FI, GB, HU, JP, KR, LU, NL, PL, RO, SE				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
AU 9214597	A1	19920827	AU 1992-14597	19920114
EP 571554	A1	19931201	EP 1992-907699	19920114
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE				

PRIORITY APPLN. INFO.: US 1991-639809 19910114
WO 1992-US356 19920114

AB Basic immunogenic peptides having epitopes for **hepatitis C** virus (**HCV**) are disclosed which are derived from the structural region of a human **HCV** genome. Preferred peptides are designated FGB1 and FGB2; sequences and characteristics are presented. Antibodies to the peptides, polynucleotide sequences encoding the peptides, vaccines contg. the peptides, and immunoassay and nucleic acid hybridization assay methods, among others, are also disclosed. FGB1 and FGB2 were made by solid-phase synthesis and used in ELISAs to **detect** antibodies to **HCV** in

blood and semen. DNA encoding FGB1 was cloned in recombinant vaccinia virus.

L12 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:590114 CAPLUS
DOCUMENT NUMBER: 117:190114
TITLE: Synthetic **antigens** for the **detection** of antibodies to **hepatitis C** virus (**HCV**)
INVENTOR(S): DeLeys, Robert J.; Pollet, Dirk; Maertens, Geert; Van Heuverswyn, Hugo
PATENT ASSIGNEE(S): Innogenetics N.V., Belg.
SOURCE: Eur. Pat. Appl., 32 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 489968	A1	19920617	EP 1990-124241	19901214
EP 489968	B1	19961106		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
EP 644202	A1	19950322	EP 1994-108611	19901214
EP 644202	B1	19970305		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 144993	E	19961115	AT 1990-124241	19901214
EP 754704	A2	19970122	EP 1996-201157	19901214
EP 754704	A3	19970528		
EP 754704	B1	19991006		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ES 2095852	T3	19970301	ES 1990-124241	19901214
AT 149522	E	19970315	AT 1994-108611	19901214
ES 2101388	T3	19970701	ES 1994-108611	19901214
AT 185350	E	19991015	AT 1996-201157	19901214
ES 2138784	T3	20000116	ES 1996-201157	19901214
IL 100158	A1	19980222	IL 1991-100158	19911126
CA 2074370	AA	19920615	CA 1991-2074370	19911213
WO 9210514	A2	19920625	WO 1991-EP2409	19911213
WO 9210514	A3	19920820		
W: AU, BR, CA, HU, JP, KR, US				
AU 9190689	A1	19920708	AU 1991-90689	19911213
AU 652013	B2	19940811		
BR 9106220	A	19930330	BR 1991-6220	19911213
JP 05503722	T2	19930617	JP 1992-500998	19911213
HU 65930	A2	19940728	HU 1992-2645	19911213
HU 218357	B	20000828		
JP 2995216	B2	19991227	JP 1991-500998	19911213
US 5922532	A	19990713	US 1995-391671	19950221
US 5910404	A	19990608	US 1995-466975	19950606
US 6007982	A	19991228	US 1995-467902	19950606
US 6287761	B1	20010911	US 1999-275265	19990323

PRIORITY APPLN. INFO.:
EP 1990-124241 A3 19901214
EP 1994-108611 A 19901214
EP 1996-201157 A 19901214
SG 1996-5024 A 19901214

	WO 1991-EP2409	A 19911213
	US 1992-920286	B1 19921014
	US 1995-391671	A3 19950221

OTHER SOURCE(S): MARPAT 117:190114

AB Synthetic peptides .gtoreq.5 amino acids long having sequences mimicking those of proteins encoded by **HCV** are prepd. for use as reagents for **screening** of blood and blood products for prior exposure to **HCV**, for **detection** of antibodies to **HCV**, for **detection** of **HCV antigens**, and as immunogens. The peptides are fragments of regions 1-92, 1688-1749, and 2263-2330 in the composite protein encoded by the **HCV** genome. The peptides may be attached to a **carrier** mol. via a linker. Thus, anti-**HCV** antibodies were **detected** in sera from patients with acute non-A, non-B hepatitis by incubation with individual peptides bound to a nylon membrane; the bound immune complexes were visualized with a goat anti-human IgG-alk. phosphatase **conjugate**, 5-bromo-4-chloro-3-indolyl phosphate, and NBT.

L12 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:136219 CAPLUS

DOCUMENT NUMBER: 116:136219

TITLE: Vaccine compositions containing alkyl compounds **conjugated** with polypeptides as immunoadjuvants

INVENTOR(S): Penny, Christopher L.

PATENT ASSIGNEE(S): North American Vaccine Inc., Can.

SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9116926	A1	19911114	WO 1991-CA144	19910501
W: AT, AU, BB, BG, BR, CA, CH, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MC, MG, MW, NL, NO, PL, RO, SD, SE, SU				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IT, LU, ML, MR, NL, SE, SN, TD, TG				
IN 172520	A	19930911	IN 1991-CA317	19910424
ZA 9103214	A	19920930	ZA 1991-3214	19910429
CA 2082425	AA	19911108	CA 1991-2082425	19910501
AU 9177779	A1	19911127	AU 1991-77779	19910501
JP 05506234	T2	19930916	JP 1991-508106	19910501
EP 597838	A1	19940525	EP 1991-908598	19910501
EP 597838	B1	19981202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
HU 65493	A2	19940628	HU 1980-92034	19910501
AT 173936	E	19981215	AT 1991-908598	19910501
ES 2124701	T3	19990216	ES 1991-908598	19910501
CN 1056816	A	19911211	CN 1991-102899	19910507
NO 9204271	A	19930107	NO 1992-4271	19921106
PRIORITY APPLN. INFO.:			US 1990-518460	19900507
			WO 1991-CA144	19910501

OTHER SOURCE(S): MARPAT 116:136219

AB An improved vaccine compn. comprising a long chain alkyl compd.

conjugated with a homogeneous immunogenic polypeptide is disclosed as an immunoadjuvant. The compns. of the invention are useful in activating the immune system to confer immunity to a host against the immunogen in a prophylactic manner. Octadecyltyrosin was **conjugated** with a homogeneous polypeptide, then injected to mice in the presence of hepatitis B surface **antigen**. Mice were boosted with polypeptide on day 21 and were bled on day 61, then the antibody concn. in the sera was **detd**. The antibody concn. at day 61 was 751 as compared to 58 ng/mL for controls with no immunoadjuvant.

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 15:54:49 ON 15 MAY 2002)

L13 13 S L9
L14 5 S L11
L15 18 S L13 OR L14
L16 12 DUP REM L15 (6 DUPLICATES REMOVED)

L16 ANSWER 1 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-114392 [15] WPIDS
DOC. NO. CPI: C2002-035137
TITLE: Soluble T cell receptor fusion or **conjugate** complexes useful in treating malignant disorders comprises either T cell receptor and polypeptide connected by a peptide linker or molecules covalently bound to a **carrier**.
DERWENT CLASS: B04 D16
INVENTOR(S): CARD, K F; WEIDANZ, J A; WONG, H C
PATENT ASSIGNEE(S): (SUNO-N) SUNOL MOLECULAR CORP
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001093913	A2	20011213	(200215)*	EN	66

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW

AU 2001075246 A 20011217 (200225)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001093913	A2	WO 2001-US18145	20010605
AU 2001075246	A	AU 2001-75246	20010605

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001075246	A Based on	WO 200193913

PRIORITY APPLN. INFO: US 2000-209536P 20000605

AN 2002-114392 [15] WPIDS
AB WO 200193913 A UPAB: 20020306
NOVELTY - Soluble T cell receptor fusion or **conjugate** complex, comprising either T cell receptor (TCR) (I) and a polypeptide connected by a peptide linker (II) or several molecules covalently bound to a **carrier** (III), is new. (I) and (II) have different recognition binding sites. (III) has at least one remaining free amine group. The **carrier** is covalently bound to a single chain T cell receptor.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) preparing soluble T cell receptor fusion or **conjugate** complex, comprising:

(a) providing T cell receptor chain or its sub-fragment;

(b) providing the polypeptide corresponding to a second chain or its sub-fragment;

(c) connecting the T cell receptor chain and the second chain to a peptide linker; and

(d) recovering the linked T cell receptor fusion polypeptide complex, thus generating a T cell receptor fusion complex;

(2) preparing soluble T cell receptor fusion or **conjugate** complex, comprising:

(a) reacting a polymer **carrier** which has covalently bound several molecules with a T cell receptor chain; and

(b) reductively stabilizing the resulting **conjugate** molecule;

(3) a nucleic acid sequence encoding the T cell receptor fusion complex comprising (I) and (II).

ACTIVITY - Cytostatic; Antiinflammatory; Immunosuppressive; Antiviral; Neuroprotective; Antidiabetic; Antirheumatic; Antiarthritic.

MECHANISM OF ACTION - TCR binder.

CTLL-2 cells were hydrodiethidium labeled and incubated for 20 minutes at room temperature (RT) with an equal number of calcein-AM labeled T2 cells pulsed with either 50 micro g of 149 or 246 peptide. The **conjugation** was observed between cells when 1 micro g of fusion protein was added to the incubation mixture containing CTLL-2 cells and 264 peptide-loaded T2 cells (i.e. 3.25 %) while **conjugate** formulation was not observed with mixture comprising the 149 peptide pulsed T2 cells used (i.e. 0.88 %).

USE - In therapeutic composition for treating disorders e.g. malignant disorder, autoimmune disorder, inflammatory response, viral infection; as **diagnostic** composition; for imaging studies (claimed). The complex is also used for the treatment of allergies and autoimmune diseases e.g. multiple sclerosis, insulin-dependent diabetes mellitus and rheumatoid arthritis, and in targeting particular tumor **antigens** in human patients. it can be used for the treatment of cancer e.g. **hepatitis C** virus (**HCV**), human immunodeficiency virus (HIV), etc, for veterinary applications e.g. treatment of disorders of livestock e.g. cattle, sheep, etc and pets such as dog and cats, and to guide, target or direct localized toxic agents to specific sites to intervene in a disease process.

ADVANTAGE - The T cell complexes teaches the use of genetic fusions and chemical **conjugation** as methods for effecting such linkage. The (TCR)-based reagents provides higher killing efficiency of tumor cells, recognizes many potential tumor

antigens as exposed on the surface of the cells or accessible to the molecule. The **antigens** recognized by antibodies are not heterogeneic in nature, thus does not limit the effectiveness of the antibody to a single tumor histology.
Dwg.0/13

L16 ANSWER 2 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2002-164292 [21] WPIDS
DOC. NO. CPI: C2002-050693
TITLE: **Hepatitis C** virus **conjugate** useful for inducing immune response in a subject comprises a polypeptides or protein complex **carrier** and immunogenic peptides covalently bonded to the **carrier**
.
DERWENT CLASS: B04 D16
INVENTOR(S): CONLEY, A J; KELLER, P M; MCKENNA, P M; PRZYSIECKI, C T
PATENT ASSIGNEE(S): (MERI) MERCK & CO INC
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001093804	A2	20011213	(200221)*	EN	63

RW: AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR
W: CA JP US

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001093804	A2	WO 2001-US17302	20010529

PRIORITY APPLN. INFO: US 2000-209089P 20000602
AN 2002-164292 [21] WPIDS
AB WO 200193804 A UPAB: 20020403
NOVELTY - **Hepatitis C** virus (**HCV**) **conjugate** comprises a polypeptide or protein complex **carrier** (a1), immunogenic **HCV** peptide PEP1 (b1), immunogenic **HCV** peptide PEP2 (c1). PEP1 and PEP2 are each covalently joined to (a1) through covalent linker and comprises different sequences as given in the specification.
DETAILED DESCRIPTION - **Hepatitis C** virus (**HCV**) **conjugate** (I) comprises a polypeptide or protein complex **carrier** (a1), immunogenic **HCV** peptide PEP1 (b1), immunogenic **HCV** peptide PEP2 (c1). PEP1 and PEP2 are each covalently joined to (a1) through a covalent linker and comprises different sequences selected from sequences Xaa-Thr-His-Thr-Thr-Gly-Gly-Gln-Ala-Gly-His-Gln-Ala-His-Ser-Leu-Thr-Gly-Leu-Phe-Ser-Pro-Gly-Ala-Lys-Gln-Asn (1), Xaa-Thr-Thr-Thr-Thr-Gly-Gly-Gln-Val-Ser-His-Ala-Thr-His-Gly-Leu-Thr-Gly-Leu-Phe-Ser-Leu-Gly-Pro-Gln-Gln-Lys (2), Xaa-Thr-Thr-Val-Val-Gly-Gly-Ser-Gln-Ser-His-Thr-Val-Arg-Gly-Leu-Thr-Ser-Leu-Phe-Ser-Pro-Gly-Ala-Ser-Gln-Asn (3), Xaa-Thr-His-Thr-Thr-Gly-Gly-Val-Val-Gly-His-Ala-Thr-Ser-Gly-Leu-Thr-Ser-Leu-Phe-Ser-Pro-Gly-Pro-Ser-Gln-Lys (4), Thr-Thr-Thr-Thr-Thr-Gly-Gly-Gln-Val-Gly-His-Gln-Thr-Ser-Gly-Leu-Thr-Gly-Leu-Phe-Ser-Pro-Gly-

Ala-Gln-Gln-Asn (5), Thr-Thr-Thr-Thr-Thr-Gly-Gly-Val-Gln-Gly-His-Thr-Thr-Arg-Gly-Leu-Val-Arg-Leu-Phe-Ser-Leu-Gly-Ser-Lys-Gln-Asn (6), Xaa-thr-His-Thr-Thr-Gly-Gly-Val-Val-Ser-His-Gln-Thr-Arg-Ser-Leu-Val-Gly-Leu-Phe-Ser-Pro-Gly-Pro-Gln-Gln-Asn (7).

Xaa = glutamine or pyroglutamide.

INDEPENDENT CLAIMS are also included for the following:

(1) an **HCV conjugate** mixture comprising (I) and a second different **HCV conjugate** (II). (II) comprises a second polypeptide or protein **carrier** (d) covalently joined to an immunogenic **HCV** peptide comprising Xaa-thr-His-Thr-Thr-Gly-Gly-Val-Val-Ser-His-Gln-Thr-Arg-Ser-Leu-Val-Gly-Leu-Phe-Ser-Pro-Gly-Pro-Gln-Gln-Asn, or their salt;

(2) production of (I) involving:

(i) joining several linkers to reactive sites on (a1);

(ii) joining two or more different **HCV** immunogenic peptides to several linkers; and

(iii) capping the product of step ii). Each of two or more different **HCV** immunogenic peptide is selected from a first to seventh **HCV** mimotope sequence comprising sequences (1) - (7); and

(3) preparation of antisera involving inoculating a subject with I/**conjugate** mixture to produce antibodies and removing the antibodies from the subject.

ACTIVITY - Virucide; Hepatotropic; Antiinflammatory.

MECHANISM OF ACTION - None given.

USE - For inducing an immune response in a subject e.g. human (claimed), chimpanzees, mice or horses; for the preparation of antisera. In therapeutic/**diagnostic** applications to generate anti-**HCV** antibodies, for **detecting** the presence of **HCV** in a subject and treating the subject infected with **HCV**.

ADVANTAGE - The **HCV conjugates** induce an immune response recognizing different strains and variants of **HCV**. The **HCV** mimotopes provide **antigens** able to generate antibodies recognizing the hypervariable region of the **HCV** E2 protein.

Dwg.0/0

L16 ANSWER 3 OF 12 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 2002-055133 [07] WPIDS

DOC. NO. CPI: C2002-015672

TITLE: Purifying complexes comprising GRP94 proteins, useful for treating a disorder associated with ischemia/reperfusion.

DERWENT CLASS: B04 D16

INVENTOR(S): NICCHITTA, C V; REED, R C; ROSSER, M F N; WASSENBERG, J J

PATENT ASSIGNEE(S): (UYDU-N) UNIV DUKE

COUNTRY COUNT: 95

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001072779	A1	20011004	(200207)*	EN	169

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE

KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO
NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ
VN YU ZA ZW
AU 2001047759 A 20011008 (200208)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001072779 A1		WO 2001-US9512	20010326
AU 2001047759 A		AU 2001-47759	20010326

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2001047759 A	Based on		WO 200172779

PRIORITY APPLN. INFO: US 2000-192118P 20000324
AN 2002-055133 [07] WPIDS
AB WO 200172779 A UPAB: 20020130
NOVELTY - Purifying a complex of a GRP94 protein, comprising contacting a complex with the GRP94 protein to bind it an agent immobilized on a solid phase support, collecting the remaining sample, and eluting the complex from the solid phase support, is new.

DETAILED DESCRIPTION - Purifying a complex of a GRP94 protein, comprising:

(a) contacting a complex comprising a GRP94 protein with a binding agent that preferentially binds GRP94, the binding agent immobilized to a solid phase support, to immobilize the complex to the solid phase support;

(b) collecting the remaining sample; and

(c) eluting the complex from the solid phase support to give purified complex in the eluate.

INDEPENDENT CLAIMS are also included for the following:

(1) isolating an antigenic molecule, associated with a GRP94 complex, comprising:

(a) contacting a complex comprising a GRP94 protein with a binding agent that preferentially binds GRP94, the binding agent immobilized to a solid phase support, to immobilize the complex to the solid phase support;

(b) collecting the remaining sample;

(c) eluting the complex from the solid phase support to give purified complex in the eluate; and

(d) isolating the antigenic molecule from the eluate;

(2) a product produced by either of the novel method, or the method of (1);

(3) **detecting** a complex comprising GRP94 in a sample suspected of containing a complex comprising GRP94, comprising:

(a) contacting the sample with a binding agent that preferentially binds GRP94 under conditions favorable to binding a complex comprising GRP94 to the binding substance to form a second complex; and

(b) **detecting** the second complex via a label **conjugated** to the binding substance or via a labeled reagent that specifically binds to the second complex subsequent to its formation;

(4) a kit for **detecting**, isolating or purifying a complex comprising GRP94 or an antigenic molecule associated with a complex comprising GRP94, the kit comprising:

(a) a binding agent that preferentially binds GRP94 contained in a first container; and

(b) an elution buffer for use in eluting a complex comprising GRP94 from the binding agent, the elution buffer contained in a second container;

(5) **screening** a candidate substance for an ability to modulate GRP94 biological activity, comprising:

(a) establishing a test sample comprising a GRP94 protein and a ligand for a GRP94 protein;

(b) administering a candidate substance to the test sample; and

(c) measuring the effect of the candidate substance on binding of the GRP94 protein and the ligand in the test sample;

(6) **screening** a candidate substance as an activator (or inhibitor) of the biological activity of a Hsp90 protein, comprising:

(a) establishing a test sample comprising a Hsp90 protein and a candidate substance;

(b) administering 1,8 -anilinonaphthalenesulfonate (8-ANS) to the test sample;

(c) **detecting** a fluorescence signal produced by the 8-ANS; and

(d) identifying the candidate substance as an activator (or inhibitor) of the biological activity of a Hsp90 protein based upon an amount of fluorescence signal produced by the 8-ANS as compared to a control sample;

(7) modulating the biological activity of a Hsp90 protein, comprising contacting a Hsp90 protein with an effective amount of a Hsp90 protein activity-modulating substance to thereby modulate the biological activity;

(8) treating a subject from a disorder where modulation of the biological activity of a GRP94 protein is desirable, comprising administering to the subject an effective amount of a GRP94 protein modulator;

(9) altering a subsequent cellular response to an ischemic condition at a tissue location in a subject, comprising treating the cells at the tissue location with a GRP94 protein modulator

(10) preparing an immunogenic composition for inducing an immune response in a vertebrate subject, comprising:

(a) harvesting from a eukaryotic cell an immunogenic complex comprising a Hsp90 protein non-covalently bound to an antigenic molecule, the complex when administered to the vertebrate subject being operative at initiating an immune response in the vertebrate subject, wherein the eukaryotic cell has been treated with an activating ligand of a Hsp90 protein; and

(b) combining the complex with a pharmaceutically acceptable carrier;

(11) preparing an immunogenic composition for inducing an immune response in a vertebrate subject, comprising:

(a) reconstituting in vitro an antigenic molecule and a Hsp90 protein molecule in the presence of a modulator of the biological activity of a Hsp90 protein to thereby produce an immunogenic complex comprising a Hsp90 protein non-covalently bound to an antigenic molecule, the complex when administered to the vertebrate subject being operative at initiating an immune response in the vertebrate subject; and

(b) combining the complex with a pharmaceutically acceptable carrier;

(12) preparing an immunogenic composition for inducing an immune response in a vertebrate subject, comprising:

(a) sensitizing one or more antigen presenting cells in vitro with a complex comprising a Hsp90 protein non-covalently bound to an antigenic molecule and with an activating ligand of a Hsp90 protein; and

(b) combining the one or more sensitized antigen presenting cells with a pharmaceutically acceptable carrier; and

(13) a product produced by one of the methods of (10)-(12).

ACTIVITY - Cardiant; Vasodilator; Hypertensive; Hyperglycemic; Anticonvulsant; Neuroprotective; Nootropic; Neuroleptic; Anxiolytic.

No biological data is given.

MECHANISM OF ACTION - GRP94 modulator.

USE - The method of (8) can be used to treat a disorder associated with ischemia/reperfusion as a result of cardiac arrest, asystole and sustained ventricular arrhythmias, cardiac surgery, cardiopulmonary bypass surgery, organ transplantation, spinal cord injury, head trauma, stroke, thromboembolic stroke, hemorrhagic stroke, cerebral vasospasm, hypotension, hypoglycemia, status eliepticus, an epileptic seizure, anxiety, schizophrenia, a neurodegenerative disorder, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis (ALS), or neonatal stress (claimed).

ADVANTAGE - None given.

Dwg.0/14

L16 ANSWER 4 OF 12 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2001251803 MEDLINE
DOCUMENT NUMBER: 21247671 PubMed ID: 11350035
TITLE: Evidence for a new **hepatitis C** virus **antigen** encoded in an overlapping reading frame.
AUTHOR: Walewski J L; Keller T R; Stump D D; Branch A D
CORPORATE SOURCE: Department of Medicine, Mount Sinai School of Medicine, New York, New York 10029, USA.
CONTRACT NUMBER: P01 DK50795 (NIDDK)
R01 DK52071 (NIDDK)
SOURCE: RNA, (2001 May) 7 (5) 710-21.
Journal code: CHB; 9509184. ISSN: 1355-8382.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010625
Last Updated on STN: 20010625
Entered Medline: 20010621

AB Many viruses have overlapping genes and/or regions in which a nucleic acid signal is embedded in a coding sequence. To search for dual-use regions in the **hepatitis C** virus (**HCV**), we developed a facile computer-based sequence analysis method to map dual-use regions in coding sequences. Eight diverse full-length **HCV** RNA and polyprotein sequences were aligned and analyzed. A cluster of unusually conserved synonymous codons was found in the core-encoding region, indicating a potential overlapping open reading frame (ORF). Four peptides (A1, A2, A3, and

A4) representing this alternate reading frame protein (ARFP), two others from the **HCV** core protein, and one from **bovine** serum **albumin** (**BSA**) were **conjugated** to **BSA** and used in western blots to test sera for specific antibodies from 100 chronic **HCV** patients, 44 healthy controls, and 60 patients with non-**HCV** liver disease. At a 1:20,000 dilution, specific IgGs to three of the four ARFP peptides were **detected** in chronic **HCV** sera. Reactivity to either the A1 or A3 peptides (both ARFP derived) was significantly associated with chronic **HCV** infection, when compared to non-**HCV** liver disease serum samples (10/100 versus 1/60; $p < 0.025$). Antibodies to A4 were not **detected** in any serum sample. Our western blot assays confirmed the presence of specific antibodies to a new **HCV** **antigen** encoded, at least in part, in an alternate reading frame (ARF) overlapping the core-encoding region. Because this novel **HCV** protein stimulates specific immune responses, it has potential value in **diagnostic** tests and as a component of vaccines. This protein is predicted to be highly basic and may play a role in **HCV** replication, pathogenesis, and carcinogenesis.

L16 ANSWER 5 OF 12 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001502009 MEDLINE
DOCUMENT NUMBER: 21437535 PubMed ID: 11553266
TITLE: Incidence of hepatitis virus infection and severe liver dysfunction in patients receiving chemotherapy for hematologic malignancies.
AUTHOR: Kawatani T; Suou T; Tajima F; Ishiga K; Omura H; Endo A; Ohmura H; Ikuta Y; Idobe Y; Kawasaki H
CORPORATE SOURCE: Second Department of Internal Medicine, Faculty of Medicine, Tottori University, Yonago, Japan.
SOURCE: EUROPEAN JOURNAL OF HAEMATOLOGY, (2001 Jul) 67 (1) 45-50.
Journal code: ERF; 8703985. ISSN: 0902-4441.
PUB. COUNTRY: Denmark
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010913
Last Updated on STN: 20011001
Entered Medline: 20010927

AB Hepatitis virus infection through virus reactivation has a high risk of mortality in patients with hematological malignancies receiving chemotherapy. We examined the incidence of both hepatitis B virus (HBV) and **hepatitis C** virus (**HCV**) infection and severe liver dysfunction (alanine aminotransferase >ten times the normal upper limit and total bilirubin >5 mg/dl) during chemotherapy in 268 patients with hematological malignancies. Eight patients (3.0%) were infected with HBV and 22 patients (8.2%) were infected with **HCV**. One patient (0.4%) was infected with both HBV and **HCV**. HBV- or **HCV**-infected patients showed severe liver dysfunction at a significantly higher incidence than non-infected patients (11/31 (35.5%) vs. 0/237 (0%), $p<0.0001$). Furthermore, the incidence of severe liver dysfunction in HBV-infected patients was significantly higher than in **HCV** -infected patients (6/8 (75.0%) vs. 4/22 (18.2%), $p<0.01$). Three of

eight HBV-infected patients were initially negative for hepatitis B surface **antigen** (HBsAg) by **latex** agglutination and became positive for HBsAg during chemotherapy. Furthermore, all three patients developed severe liver dysfunction and two developed fatal fulminant hepatitis. From an examination of the original stock of serum samples before chemotherapy, two patients were found to be positive for HBV-DNA by polymerase chain reaction (PCR). Although post-transfusion HBV infection was suspected in the one remaining patient, the cause of HBV infection could not be clarified due to the impossibility of examination in blood donors. Since HBV-infected patients develop severe liver dysfunction at a higher incidence than either patients not infected with virus or **HCV**-infected patients before chemotherapy for hematological malignancies, it is recommended that HBV-DNA should be tested by PCR to **detect** HBV marker-negative **carriers** and liver function tests should be carefully monitored.

L16 ANSWER 6 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 2000-053080 [04] WPIDS
DOC. NO. NON-CPI: N2000-041367
DOC. NO. CPI: C2000-013784
TITLE: New peptides useful for prophylactic and therapeutic treatment of **hepatitis C**.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): BARBAN, V
PATENT ASSIGNEE(S): (INMR) PASTEUR MERIEUX SERUMS & VACCINS SA
COUNTRY COUNT: 86
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9958561	A1	19991118	(200004)*	FR	45
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ UG ZW					
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZA ZW					
AU 9937144	A	19991129	(200018)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9958561	A1	WO 1999-FR1155	19990514
AU 9937144	A	AU 1999-37144	19990514

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9937144	A	Based on	WO 9958561

PRIORITY APPLN. INFO: FR 1998-6335 19980514
AN 2000-053080 [04] WPIDS
AB WO 9958561 A UPAB: 20000124
NOVELTY - A peptide (I) for the prophylactic and therapeutic

treatment of **hepatitis C** is new and is capable of reacting with a specific antibody of an **antigen** comprising the **hepatitis C** viral structure.

DETAILED DESCRIPTION - A peptide (I) for the prophylactic and therapeutic treatment of **hepatitis C** is new and is capable of reacting with a specific antibody of an **antigen** comprising the **hepatitis C** viral structure. The peptide comprises an amino acid sequence that imitates a conformational epitope of the antigenic structure of the virus without wholly corresponding to an amino acid sequence of this **antigen** comprising sequences (I) - (VII):

(I) Gln-Leu-Ile-Thr-Lys-Pro-Leu;
(II) His-Ala-Phe-Pro-His-Leu-His;
(III) Ser-Ala-Pro-Ser-Ser-Lys-Asn;
(IV) Gly-Glu-Thr-Arg-Ala-Pro-Leu;
(V) Ser-Val-Ser-Val-Gly-Met-Lys-Pro-Ser-Pro-Arg-Pro;
(VI) Trp-Gln-Ser-Tyr-Pro-Met-Phe-Asn-Asn-Thr-Leu-Thr;
(VII) Met-Leu-Pro-Ser-Val-Leu-Asp.

INDEPENDENT CLAIMS are also included for the following:

(1) a **conjugate** comprising at least one (I) linked to a molecule to introduce or reinforce the immunogenicity of the peptide;

(2) a recombinant vector comprising a functional expression cassette allowing for the expression of a polynucleotide coding for (I);

(3) a therapeutic and/or prophylactic composition for **hepatitis C** for use as a vaccine comprising (I) as an active ingredient, optionally **conjugated**, and/or a recombinant vector coding for (I); and

(4) use of (I) as a reagent for the **diagnosis** of **hepatitis C** and/or the susceptibility to chronic infection by **hepatitis C** viral infection comprising the **determination** of a humoral response and/or specific cellular mediation of (I) using a whole blood sample.

USE - The peptide(s) (I) is useful for the preparation of a therapeutic and/or prophylactic composition for the treatment and/or prevention of **hepatitis C**, especially for use as a vaccine comprising (I) (optionally **conjugated**) and/or a recombinant vector coding for (I). Also (I) is useful as a reagent for the **diagnosis** of **hepatitis C** and/or the susceptibility to chronic infection by the **hepatitis C** virus comprising the **determination** of a humoral and/or specific cellular mediated response of (I) on a whole blood sample (all claimed).

ADVANTAGE - The pharmaceutical composition is used to efficiently treat or prevent **hepatitis C** infection and is useful for the distinction between **carriers**, those chronically infected patients and those ho have been cured of a previous infection. The antibodies are easily reproduced having the same characteristics of CDR by recombinant mutagenesis or cloning.

Dwg.0/4

L16 ANSWER 7 OF 12 MEDLINE
ACCESSION NUMBER: 1999435620 MEDLINE
DOCUMENT NUMBER: 99435620 PubMed ID: 10507763
TITLE: The asialoglycoprotein receptor in human hepatocellular carcinomas: its expression on

proliferating cells.

AUTHOR: Trere D; Fiume L; De Giorgi L B; Di Stefano G; Migaldi M; Derenzini M

CORPORATE SOURCE: Servizio di Citopatologia, Policlinico S Orsola, and Dipartimento di Patologia Sperimentale, Universita di Bologna, Italy.

SOURCE: BRITISH JOURNAL OF CANCER, (1999 Oct) 81 (3) 404-8. Journal code: AV4; 0370635. ISSN: 0007-0920.

PUB. COUNTRY: SCOTLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199910

ENTRY DATE: Entered STN: 19991026
Last Updated on STN: 19991026
Entered Medline: 19991014

AB The expression of the asialoglycoprotein receptor (ASGP-R) on human hepatocellular carcinoma (HCC) cells might be exploited to reduce the extrahepatic toxicity of DNA synthesis inhibitors by their **conjugation** with galactosyl-terminating peptides. In the present study we first assessed the frequency of ASGP-R expression in 60 HCCs. Secondly, we investigated whether the receptor was maintained on the plasma membranes of DNA synthesizing cancer cells. Needle biopsies of HCC were evaluated. **Diagnosis** and grading of HCC were performed on routine haematoxylin and eosin-stained sections according to Edmondson and Steiner (1953). Thirty-five tumours were grade I and II and were classified as well differentiated, while 25 tumours were grade III and IV and were classified as poorly differentiated. Sections from formalin-fixed, paraffin-embedded samples were incubated, after **antigen** retrieval, with an anti-ASGP-R monoclonal antibody revealed by secondary biotinylated antibody and streptavidin-biotin-peroxidase-diaminobenzidine reaction. A clear immunolabelling of plasma membranes of HCC cells was observed in 28 out of 35 (80%) well differentiated (grade I and II) and in five out of 25 (20%) poorly differentiated (grade III and IV) HCCs. The presence of the ASGP-R on the surface of DNA synthesizing cancer cells was also investigated after in vitro bromodeoxyuridine (BrdU) labelling of HCC samples by immunohistochemical visualization of both the ASGP-R and incorporated BrdU on the same section. The results obtained clearly demonstrated that DNA synthesizing cancer cells expressed the ASGP-R on their surface. The presence of ASGP-R on cell plasma membrane in the majority of differentiated HCCs and its maintenance on proliferating cells encourages studies in order to restrict the action of the inhibitors of DNA synthesis of HCC cells by their **conjugation** with galactosyl-terminating **carriers** internalized through this receptor.

L16 ANSWER 8 OF 12 WPIDS (C) 2002 THOMSON DERWENT

ACCESSION NUMBER: 1997-538749 [50] WPIDS

DOC. NO. NON-CPI: N1997-448356

DOC. NO. CPI: C1997-172420

TITLE: Reagent for **diagnosis** of **hepatitis C** virus infections - comprises solid phase sensitised with **conjugate** of **antigen** and **carrier** protein, useful in, e.g. measurements by forward-scattered light flow

cytometry.
DERWENT CLASS: A96 B04 D16 S03
INVENTOR(S): SHIRAISHI, K; TAKAHAMA, Y; SHIRAISHI, J
PATENT ASSIGNEE(S): (TOAM-N) TOA MEDICAL ELECTRONICS CO LTD; (SYSM-N) SYSMEX CORP; (TOAI-N) TOA IYO DENSHI KK
COUNTRY COUNT: 7
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 806669	A2	19971112	(199750)*	EN	11
R: BE DE FR GB IT					
JP 09297141	A	19971118	(199805)		8
EP 806669	A3	19971126	(199816)		
KR 97075910	A	19971210	(199848)		
EP 806669	B1	20020410	(200227)	EN	
R: BE DE FR GB IT					

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 806669	A2	EP 1997-107368	19970505
JP 09297141	A	JP 1996-112442	19960507
EP 806669	A3	EP 1997-107368	19970505
KR 97075910	A	KR 1997-16607	19970430
EP 806669	B1	EP 1997-107368	19970505

PRIORITY APPLN. INFO: JP 1996-112442 19960507
AN 1997-538749 [50] WPIDS
AB EP 806669 A UPAB: 19971217
Reagent for **diagnosis** of **hepatitis C** virus (**HCV**) infection obtained by sensitising a solid phase with a **conjugate** prepared by chemical bonding of an **HCV antigen** and a **carrier** protein is new. Also claimed is a method of **diagnosing HCV** infection comprising: (a) adding the reagent to the sample, and (b) measuring the degree of agglutination of the **carrier** particles.

USE - The method uses a **diagnostic** reagent for **detecting HCV** infection by utilising immunoagglutination. When the solid phase comprises **carrier** particles, the reagent can be used in an agglutination assay, especially in which the degree of agglutination is **determined** by measuring forward-scattered light in a flow cytometer (claimed).

ADVANTAGE - The agglutination assay is more sensitive (capable of **detecting** an infection at an earlier stage) than conventional passive haemagglutination and ELISA assays.
Dwg.0/0

L16 ANSWER 9 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1994-129040 [16] WPIDS
DOC. NO. NON-CPI: N1994-101241
DOC. NO. CPI: C1994-059563
TITLE: Reagent for antibody **determn.** esp. of **hepatitis C** virus - contg.

antigen or peptide with thiol gp., with reagent contg. or treated with reducing agent.
DERWENT CLASS: B04 D16 S03
PATENT ASSIGNEE(S): (DAIN-N) DAINABOT CO LTD
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
JP 06074956	A	19940318	(199416)*		8
JP 3225468	B2	20011105	(200172)		8

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
JP 06074956	A	JP 1992-270684	19920828
JP 3225468	B2	JP 1992-270684	19920828

FILING DETAILS:

PATENT NO	KIND		PATENT NO
JP 3225468	B2	Previous Publ.	JP 06074956

PRIORITY APPLN. INFO: JP 1992-270684 19920828
AN 1994-129040 [16] WPIDS
AB JP 06074956 A UPAB: 19940608
The antibody immunoassays contains an **antigen** which has a sensitive thiol group or peptide having the same effect; The reagent contains a reducing agent; or the reagent is treated with a reducing agent.

Pref. the reducing agent is antioxidant of thiol group, esp. dithiothreitol, dithioerythritol and/or thioglycolic acid, etc.; The **antigen** is **HCV antigen** or the NS3 region of non-structural region of **HCV** genome; The reagent contains **carrier** comprising tubes, plates, erythrocytes or **latex** particles.

By containing a reducing agent in the reagent or by treating the reagent with a reducing agent, the sensitivity of the reagent for the **determination** can be raised.

USE/ADVANTAGE - The invention relates to a reagent for the **determination** of antibody, esp. antibody to **hepatitis C** virus (**HCV**). **HCV** antibody can be accurately **determined** with high sensitivity.
Dwg.0/0

L16 ANSWER 10 OF 12 JAPIO COPYRIGHT 2002 JPO
ACCESSION NUMBER: 1991-287069 JAPIO
TITLE: MEASURING REAGENT
INVENTOR: ARIMA TERUMASA; YAMADA KYOKO; HATANAKA TADASHI; NANBA TOSHIHIKO; TSUJI MASAO
PATENT ASSIGNEE(S): KURARAY CO LTD, JP (CO 000108)
ARIMA TERUMASA, JP (IN)
PATENT INFORMATION:

PATENT NO	KIND	DATE	ERA	MAIN IPC

JP 03287069 A 19911217 Heisei (5) G01N033-576

JP
APPLICATION INFORMATION
ST19N FORMAT: JP1990-88892 19900402
ORIGINAL: JP02088892 Heisei
SOURCE: PATENT ABSTRACTS OF JAPAN, Unexamined Applications, Section: P, Sect. No. 1328, Vol. 16, No. 117, P. 121 (19920324)
AN 1991-287069 JAPIO
AB PURPOSE: To specifically **detect** an antibody (**HCV** antibody) having specificness to non-A non-B type hepatitis-associated **antigen** with a high sensitivity and high degree by consisting the above measuring reagent of peptide having the amino acid array expressed by specific formula. CONSTITUTION: The peptide having the amino acid array expressed by the formula I is synthesized by a solid phase synthesis method to obtain the measuring reagent of the **HCV** antibody. A **carrier** is coated with this measuring reagent as an **antigen** material and thereafter, a block agent is acted to block the nonspecific protein **conjugated** section on the **carrier**. A sample to be inspected is added to the **carrier** coated with the measuring reagent and is incubated. An enzyme labeled antibody is then brought into contact therewith and the **carrier** is incubated. A substrate is added to the **carrier** treated in such a manner and the **carrier** is incubated. The decomposed quantity of the **carrier** is measured by using an absorptiometer. The **HCV** antibody to the non-A non-B type hepatitis-associated **antigen** after blood transfusion is **detected** specifically with the high sensitivity in this way.

L16 ANSWER 11 OF 12 MEDLINE
ACCESSION NUMBER: 87110768 MEDLINE
DOCUMENT NUMBER: 87110768 PubMed ID: 2949020
TITLE: An enzyme-linked immunosorbent assay (ELISA) for the **detection** of IgG and IgM anti-idiotypes directed against anti-HBs molecules.
AUTHOR: Irshad M; Gandhi B M; Acharya S K; Joshi Y K; Tandon B N
SOURCE: JOURNAL OF IMMUNOLOGICAL METHODS, (1987 Feb 11) 96 (2) 211-7.
Journal code: IFE; 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198703
ENTRY DATE: Entered STN: 19900303
Last Updated on STN: 19980206
Entered Medline: 19870326
AB A simple and specific enzyme-linked immunosorbent assay (ELISA) has been developed to **detect** circulating IgG and IgM anti-idiotypic antibodies directed against anti-HBs molecules using 96-well polyvinyl microtitre plates as the solid phase and HRPO-labelled goat anti-HBs as **conjugate**. Anti-idiotype reactions were observed in the supernatant portion after

precipitation of immune complexes from sera with polyethylene glycol 6000 (PEG). Both IgG and IgM with anti-idiotype activity were **detected** concurrently in HBsAg-positive sera from HBV-infected patients and asymptomatic HBV **carriers**. Anti-idiotype activity was absent in HBsAg-negative sera from healthy persons, and in patients with non-A, non-B hepatitis and viral hepatitis A. However, such antibodies could be demonstrated in the sera of two out of eight HBsAg vaccine recipients negative for anti-HBs but in none of 11 recipients positive for anti-HBs after receiving a booster immunising dose of HBsAg vaccine. Those sera showing positive anti-idiotype reactions were free from rheumatoid factor and HBsAg/IgM or HBsAg/IgG complex activity. An analysis of anti-idiotype positive sera for anti-HBs, HBeAg and HBV-specific DNA-polymerase activity demonstrated these markers in 20%, 30% and 60% of cases, respectively. The presence of anti-idiotypic antibodies was presumed to permit a more active multiplication of hepatitis B virus.

L16 ANSWER 12 OF 12 WPIDS (C) 2002 THOMSON DERWENT
ACCESSION NUMBER: 1983-32501K [14] WPIDS
DOC. NO. NON-CPI: N1983-058771
DOC. NO. CPI: C1983-031705
TITLE: Polypeptide(s) mfr. with hepatitis B virus E **antigen** antigenicity - useful in antibody formation for **detection** and treatment of hepatitis.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MACKAY, P; MURRAY, K
PATENT ASSIGNEE(S): (BIOG) BIOGAL GYOGYSZERGYAR; (BIOJ) BIOGEN NV
COUNTRY COUNT: 22
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 75395	A	19830330	(198314)*	EN	27
R: AT BE CH DE FR GB IT LI LU NL SE					
AU 8287465	A	19830310	(198316)		
JP 58052228	A	19830328	(198318)		
FI 8203021	A	19830429	(198323)		
DK 8203896	A	19830530	(198328)		
ZA 8206310	A	19830518	(198337)		
ES 8404186	A	19840716	(198438)		
US 4563423	A	19860107	(198605)		
CA 1209502	A	19860812	(198637)		
US 4758507	A	19880719	(198831)		
IL 66670	A	19890515	(198926)		
JP 06194368	A	19940715	(199433)		10
JP 06194369	A	19940715	(199433)		10

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 4563423	A		US 1982-414439	19820902
US 4758507	A		US 1985-784115	19851004
JP 06194368	A	Div ex	JP 1982-149377	19820830
			JP 1992-283453	19820830
JP 06194369	A	Div ex	JP 1982-149377	19820830

JP 1992-283454 19820830

PRIORITY APPLN. INFO: GB 1981-26583 19810902
AN 1983-32501K [14] WPIDS
AB EP 75395 A UPAB: 19930925
Prodn. of a polypeptide(s) displaying the antigenicity of hepatitis B virus e **antigens** (HBeAg) comprises prepn. of a bacterial extract of a host characterised by the expression of a polypeptide displaying the antigenicity of hepatitis B virus core **antigen**. Then the extract is digested with a protease in presence of a reducing agent (I) (the protease is resistant to (I)). (I) is suitably 2-mercaptoethanol, dithiothreitol, glutathione, dithioerythritol, a thioglycollate or NaBH4. The protease is esp. pronase, subtilis, carboxypeptidase, A or B, papain, trypsin, chymopapain, bromelin, protease K or thermo-lysin. For the procedure of paragraph (B) (I) is esp. 2-mercapto-ethanol and the dissociating conditions are produced by Na dodecylsulphate.

HBeAg can be produced efficiently and in large amts., and the antibodies can be similarly obtd., and they are not contaminated and are suitable for use in the identification of hepatitis B virus infective **carriers** and in the **determn**. of the course of hepatitis B virus related liver diseases and then treatment by inclusion in vaccines.

ABEQ US 4563423 A UPAB: 19930925
Prepn. of a polypeptide (I) displaying the antigenicity of **hepatitis** B virus **C antigens** comprises first preparing a bacterial extract of a host characterised by the expression of a polypeptide displaying the antigenicity of hepatitis B virus core **antigen**. The extractis digested with a reducing agent resistant protease in the presence of a reducing agent to convert the polypeptide displaying the antigenicity of hepatitis B virus core **antigen** into a polypeptide (I).

USE - (I) and its antibodies are used to **detect** hepatitis B virus infection, esp. for finding carriersand in evaluating the course of HBV-related chronic liver disease.

ABEQ US 4758507 A UPAB: 19930925
Polypeptide with hepatitis B e-antigenic properties is new. Prepn. of this polypeptide comprises expression of the polypeptide in a host microorganism which has been modified with a suitable plasmid; isolation of the bacterial extract contg. the polypeptide; and digestion of the extract with a protease which is resistant to reducing agent in the presence of the reducing agent, converting the core **antigen** to an e-**antigen**.

USE - The prod. has the antigenic activity of hepatitis B virus e-**antigens**, without corresp. virus surface **antigen** activity and is a reagent for the **detection** of the **conjugate** antibodies in blood serum or liver tissues.

=> fil hom
FILE 'HOME' ENTERED AT 15:59:01 ON 15 MAY 2002

(FILE 'MEDLINE' ENTERED AT 14:14:42 ON 16 MAY 2002)
L1 8224 SEA FILE=MEDLINE ABB=ON PLU=ON "HEPATITIS C VIRUS"/CT
L2 47795 SEA FILE=MEDLINE ABB=ON PLU=ON ANTIGENS/CT
L3 9 SEA FILE=MEDLINE ABB=ON PLU=ON L1 AND L2

L3 ANSWER 1 OF 9 MEDLINE
AN 2002052474 MEDLINE
TI Preliminary classification of nonmalignant B cell proliferation in Sjogren's syndrome: perspectives on pathobiology and treatment based on an integrated clinico-pathologic and molecular study approach.
AU De Vita S; De Marchi G; Sacco S; Gremese E; Fabris M; Ferraccioli G
SO BLOOD CELLS, MOLECULES, AND DISEASES, (2001 Jul-Aug) 27 (4) 757-66. Ref: 53
Journal code: 9509932. ISSN: 1079-9796.
AB A classification of nonmalignant lymphoproliferation in Sjogren's syndrome is presented, based on the results of international meetings regarding Sjogren's syndrome-associated lymphomagenesis and on our results of a clinico-pathologic and molecular study and long-term follow-up in well-characterized patients. Sjogren's syndrome pathobiology has similarities to hepatitis C virus-related B-cell lymphoproliferation. Antigen stimulation with the preferential expansion of rheumatoid factor-positive clones and specific immunoglobulin gene expression and recombination represent key biologic events in lymphoproliferation. This classification is based on the coupling of molecular and histological studies and may result in more selective treatment approaches.

L3 ANSWER 2 OF 9 MEDLINE
AN 2001515198 MEDLINE
TI DNA vaccination: a potential weapon against infection and cancer.
AU Stevenson F K; Rosenberg W
SO VOX SANGUINIS, (2001 Jan) 80 (1) 12-8. Ref: 51
Journal code: XLI; 0413606. ISSN: 0042-9007.
AB DNA vaccination is a novel approach for inducing immunity against target antigens. It provides a direct link between identification of genes encoding these antigens and incorporation of the gene sequences into a vaccine vehicle. Identification of candidate genes is proceeding very rapidly both for infectious organisms and for cancer cells. One advantage is that DNA appears to activate all pathways of immunity, especially cytotoxic T-cell responses, which have been difficult to induce with protein vaccines. For viruses, including those which have caused problems for blood transfusion, DNA vaccination could be used for prevention. However, for chronic infection, or for cancer, vaccination will be performed in a therapeutic setting. For this situation, it is probable that immune-activating sequences will have to be included in the vaccine. The ease of manipulation of gene sequences, together with the increasing knowledge of the operation of the immune system, means that we now have the tools to take vaccines into the next exciting stage of development.

L3 ANSWER 3 OF 9 MEDLINE
AN 2001425098 MEDLINE
TI The GOR gene product cannot cross-react with hepatitis C virus in humans.
AU Koike R; Iizuka T; Watanabe T; Miyasaka N
SO CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (2001 Jun) 124 (3) 429-34.

Journal code: DD7; 0057202. ISSN: 0009-9104.

AB GOR (GOR47--1) is an epitope thought to be a host-derived antigen cross-reactive with hepatitis C virus (HCV) since it was isolated from a cDNA library of host animals reactive with sera of HCV-positive patients. An enzyme immunosorbent assay (ELISA) using this epitope as antigen is of sufficient sensitivity and specificity for screening patients with HCV. However, the relationship between GOR47--1 epitope and autoimmune phenomena associated with HCV infection or autoimmune hepatitis is controversial. Here we isolated the human GOR gene and found that the GOR47--1 epitope was not translated in humans due to a single base replacement from chimpanzee. Furthermore, we found some patients who had antibodies against another epitope, which is translated (GOR1--125) in humans, although there was no correlation between the existence of anti-GOR47--1 or anti-GOR1--125 Ab and autoimmune phenomena. Serum IgG levels did not influence the titres of these antibodies. Taken together with the results of several other studies, our finding that the GOR47--1 epitope cannot be translated into a protein suggests that there is little relationship between autoimmunity and the GOR gene product in human beings. We also discuss here the possible mechanism of cross-reactivity between HCV and the GOR gene product.

L3 ANSWER 4 OF 9 MEDLINE
AN 1998295835 MEDLINE
TI Infection of a chimpanzee with hepatitis C virus grown in cell culture.
AU Shimizu Y K; Igarashi H; Kiyohara T; Shapiro M; Wong D C; Purcell R H; Yoshikura H
SO JOURNAL OF GENERAL VIROLOGY, (1998 Jun) 79 (Pt 6) 1383-6.
Journal code: I9B; 0077340. ISSN: 0022-1317.
AB Culture supernatant harvested from Daudi cells, a lymphoplastoid cell line, after 58 days of infection with the H77 strain of hepatitis C virus (HCV), was inoculated into a chimpanzee. HCV RNA, as detected by RT-PCR, first appeared in the serum and liver 5 and 6 weeks, respectively, after inoculation. Peripheral blood mononuclear cells (PBMC) collected on week 7 were also positive for HCV RNA. The major sequences of hypervariable region 1 (HVR1) of the viral genome recovered from the inoculated chimpanzee were the ones which were the majority in the original H77 inoculum and not those which were in the majority in the culture supernatant. Only the sequence recovered from PBMC was the same as the major one found in the cell culture.

L3 ANSWER 5 OF 9 MEDLINE
AN 96078149 MEDLINE
TI Passive adsorption of immunologically active and inactive synthetic peptides to polystyrene is influenced by the proportion of non-polar residues in the peptide.
AU Sallberg M; Blixt M; Zhang Z X; Ekstrand J
SO IMMUNOLOGY LETTERS, (1995 May) 46 (1-2) 25-30.
Journal code: GIH; 7910006. ISSN: 0165-2478.
AB A well-known drawback in the use of synthetic peptides as solid-phase antigens in immunoassays is that positive controls confirming the presence of the peptide on the solid phase are not always present. We therefore evaluated the applicability of a recently described enzyme immunoassay (EIA) method by which the presence of peptides is detected by biotinylation (BioEIA) of alpha- and/or epsilon-amino groups after passive adsorption. This approach

allows the rapid screening of a large number of proteins and peptides in respect to passive adsorption to plastic surfaces. When using irradiated polystyrene microplates we found that 240 (94%) of 256 synthetic peptides, covering 85% of the complete hepatitis C virus (HCV) sequence, passively adsorbed to polystyrene. When comparing the results from the BioEIA to the peptide reactivity of human sera it was obvious that the absence of serum reactivities was not due to lack of peptide adsorption to the plates. Using 192 peptides the relation between the signal-to-cutoff ratio (S/CO) in the BioEIA and the amino acid content of the individual peptides was further analyzed. The S/CO ratio was related to the number of epsilon NH2 groups (Lys residues) present in the peptide ($P < 0.001$, Kruskal-Wallis). We separately related the amino acid content of 68 peptides with Lys and 124 peptides lacking Lys to the S/CO ratio in the BioEIA. In both cases it was found that an increasing amount of nonpolar residues such as Ala, Phe, Ile, Met, and Val ($P < 0.05$, respectively) in the peptides was related to a lower S/CO ratio in the BioEIA.(ABSTRACT TRUNCATED AT 250 WORDS)

L3 ANSWER 6 OF 9 MEDLINE
AN 95010078 MEDLINE
TI Induction of the human gene for p44, a hepatitis-C-associated microtubular aggregate protein, by interferon-alpha/beta.
AU Kitamura A; Takahashi K; Okajima A; Kitamura N
SO EUROPEAN JOURNAL OF BIOCHEMISTRY, (1994 Sep 15) 224 (3) 877-83.
Journal code: EMZ; 0107600. ISSN: 0014-2956.
AB A hepatitis-C-associated microtubular aggregate protein, referred to as p44, has been identified as a cytoplasmic antigen in the hepatocytes of chimpanzees infected with hepatitis C virus. The production of p44 mRNA is markedly induced in the liver of chimpanzees infected with hepatitis C or hepatitis D virus. To examine the mechanism of this induction, we isolated a genomic clone for the human p44 protein and analyzed its structure. The human p44 gene spans approximately 14 kbp of DNA and consists of nine exons separated by eight introns. An interferon-stimulated response element, which confers inducibility by interferon-alpha/beta, was found in the promoter region of the gene. Northern-blot analysis revealed that the human p44 gene is inducible by interferon-alpha/beta, but not by interferon-gamma. Functional analysis demonstrated that the interferon-stimulated response element in the promoter region of the gene mediates the inducibility of the gene by interferon-alpha/beta. Thus, the human p44 gene is a member of the family of interferon-alpha/beta inducible genes. The protein p44 may be one of the mediators involved in the antiviral action of interferon.

L3 ANSWER 7 OF 9 MEDLINE
AN 94143940 MEDLINE
TI Evaluation of indeterminate c22-3 reactivity in volunteer blood donors.
AU Tobler L H; Busch M P; Wilber J; Dinello R; Quan S; Polito A; Kochesky R; Bahl C; Nelles M; Lee S R
SO TRANSFUSION, (1994 Feb) 34 (2) 130-4.
Journal code: WDN; 0417360. ISSN: 0041-1132.
AB BACKGROUND: Approximately 25 percent of blood donor sera that are repeatably reactive for hepatitis C virus (HCV) on second-generation enzyme immunoassay (EIA 2.0) are indeterminate on second-generation recombinant immunoblot assay (RIBA 2.0), and over 76 percent of

these results are due to single reactivity to the HCV recombinant antigen c22-3. STUDY DESIGN AND METHODS: Data are presented on 46 volunteer allogeneic blood donors who were reactive on EIA2.0 and c22-3 indeterminate in RIBA 2.0. Index and follow-up samples were evaluated by using a panel of five synthetic peptide EIAs, a prototype strip immunoblot assay that uses synthetic peptides in addition to recombinant protein (RIBA 3.0), and polymerase chain reaction (PCR) for HCV RNA. RESULTS: All 46 donations had normal alanine aminotransferase values; only 2 (4.3%) reacted for antibody to hepatitis B core antigen. With a panel of 12 synthetic peptides spanning the entire sequence of the c22-3 recombinant antigen, 33 plasmas (72%) reacted to one peptide or none, including 19 plasmas with reactivity restricted entirely to the N-terminal peptide (1-15 amino acids) of c22-3. With RIBA 3.0, 28 donations (61%) were nonreactive, including 25 that reacted with one peptide or none in EIA. Of these 25 plasmas, 18 reacted with the N-terminal sequence only. All 46 index donations were tested by PCR; the single PCR-positive unit reacted with four HCV peptides, was positive by RIBA 3.0, and reacted for antibody to hepatitis B core antigen. Twenty-six index donors were successfully recalled 3 to 7 months after their index donation. None seroconverted to positivity in RIBA 2.0, 1 was nonreactive, and 25 remained positive for c22-3 only. The restricted epitope reactivity in peptide EIA and RIBA 3.0 was maintained over time in all cases. All 26 of the follow-up samples tested negative by PCR. CONCLUSION: On the basis of the restricted peptide reactivity and PCR negativity of index and follow-up samples, it is concluded that the majority of c22-3 RIBA 2.0-indeterminate results are due to nonspecific cross-reactivity to restricted (principally, N-terminal) regions of HCV core antigen.

L3 ANSWER 8 OF 9 MEDLINE
AN 91011346 MEDLINE
TI Cloning, sequencing and expression in Escherichia coli of cDNA for a non-A, non-B hepatitis-associated microtubular aggregates protein.
AU Takahashi K; Kitamura N; Shibui T; Kamizono M; Matsui R; Yoshiyama Y; Maeda T; Kondo J; Honda Y; Yamada E; +
SO JOURNAL OF GENERAL VIROLOGY, (1990 Sep) 71 (Pt 9) 2005-11. Journal code: I9B; 0077340. ISSN: 0022-1317.
AB A 1.7 kb cDNA encoding a novel antigen (p44; apparent Mr 44K) associated with non-A, non-B (NANB) hepatitis, was isolated from the hepatic cDNA library of a chimpanzee infected with NANB hepatitis. The library was screened with a monoclonal antibody against this antigen. The cDNA cloned contained an open reading frame encoding a 444 amino acid protein with an Mr calculated to be 50,468. The cDNA hybridized to a 1.9 kb mRNA obtained from chimpanzee hepatocytes infected with either the NANB or hepatitis delta viruses. It hybridized weakly to mRNA from hepatitis B virus-infected hepatocytes, and not at all to mRNA from normal chimpanzee hepatocytes. Southern blot analysis revealed that p44 is a host protein in chimpanzees, and that an identical gene exists in the human genome.

L3 ANSWER 9 OF 9 MEDLINE
AN 91011345 MEDLINE
TI Isolation and purification of a non-A, non-B hepatitis-associated microtubular aggregates protein.
AU Honda Y; Kondo J; Maeda T; Yoshiyama Y; Yamada E; Shimizu Y K; Shikata T; Ono Y

SO JOURNAL OF GENERAL VIROLOGY, (1990 Sep) 71 (Pt 9) 1999-2004.
Journal code: I9B; 0077340. ISSN: 0022-1317.

AB Blood-borne type non-A, non-B (NANB) hepatitis-associated microtubular aggregates protein was isolated and partially sequenced. The microtubular aggregates were isolated from the hepatocytes of NANB-infected chimpanzees and were found to have a buoyant density in sucrose solution of 1.21 to 1.23 g/ml. A single protein, recognized by our anti-microtubular aggregates monoclonal antibodies, was found to have an Mr of 44,000 (p44). This p44 protein was not found in uninfected chimpanzees. We determined a partial amino acid sequence for p44, and showed that it has no homology to any known proteins.

=> fil hom
FILE 'HOME' ENTERED AT 14:15:30 ON 16 MAY 2002